Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Genetics & Development

Editorial overview: Cell reprogramming, regeneration and repair: Reprogramming: the eternal circle

Amander T Clark and Thomas P Zwaka

Current Opinion in Genetics & Development 2015, **34**:v–vi

For a complete overview see the Issue

Available online 20th October 2015

http://dx.doi.org/10.1016/j.gde.2015.09.006

Amander T Clark
University of California Los Angeles, Department of Molecular Cell and Developmental Biology, Los Angeles, CA 90095, USA
e-mail: clarka@ucla.edu

Amander Clark is a member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at the University of California, Los Angeles. She obtained her PhD from the University of Melbourne, Australia, and did her postdoctoral training with Renee Reijo-Pera at the University of California, San Francisco. Clark is currently Professor and Vice Chair, Department of Molecular Cell and Developmental Biology at the University of California, Los Angeles.

Thomas P Zwaka
Icahn School of Medicine at Mount Sinai, Black Family Stem Cell Institute, One Gustave L. Levy Place, New York, NY 10028, USA
e-mail: thomas.zwaka@mssm.edu

Thomas Zwaka is a member of the Black Family Stem Cell Institute in New York. He obtained his MD and PhD from the University of Ulm in Germany and did his postdoctoral training in Jamie Thomson's laboratory at the University of Wisconsin, Madison. Zwaka is currently a Professor in the Department of Developmental and Regenerative Biology, Icahn School of Medicine at Mount Sinai, New York, NY.

"We dance round in a ring and suppose,
But the Secret sits in the middle and knows."

—Robert Frost

Reprogramming is as old as life itself. Even the most archaic protocells dissembled and reassembled their structures to rejuvenate or radically alter their lipid, salt and ribonucleic acid composition. Reprogramming is fascinating to us because it forces us to contemplate fates where past and future, cause and effect are neither categorical nor unidirectional.

In this edition of *COGEDE*, we have invited colleagues to contribute their unique perspectives to illustrate the diverse ways that reprogramming is used in biology. This includes studying or harnessing reprogramming in various model systems as well as different experimental and natural contexts. Our goal is to demonstrate that reprogramming is not restricted to one stage of life, and it is not exclusively an *in vitro* or an *in vivo* phenomenon.

The most extreme example of cellular reprogramming in mammals occurs naturally during fertilization: the specialized epigenome of each haploid gamete is converted into the totipotent diploid epigenome of the pre-implantation embryo. In this edition, Miguel Ramalho-Santos and colleagues describe the chromatin changes that guide this conversion, while Amander Clark provides mechanistic insight into DNA methylation remodeling, and how it relates to other types of *in vivo* and *in vitro* reprogramming.

Epigenetic reprogramming by the oocyte has been harnessed experimentally in somatic cell nuclear transfer to generate cloned animals or cloned embryonic stem cell lines. Dieter Egli and colleagues were among the first to successfully generate cloned human pluripotent stem cell lines using this method, and their review gives us a succinct history of somatic cell nuclear transfer since John Gurdon's success in cloning frogs 50 years ago.

One of the major goals of experimental reprogramming in the last decade has focused on the generation of pluripotent stem cell lines. However, in the past several years we now appreciate that pluripotency is a spectrum of states, from naïve pluripotency in pre-implantation blastocysts to primed pluripotency that can be coaxed out of cells from the post-implantation mouse embryo. The challenge to this basic paradigm is that human pluripotent stem cells exhibit a closer relationship to primed mouse pluripotent

stem cells, yet are derived from the pre-implantation blastocyst. Qi-Long Ying and colleagues shed light on this paradox by explaining that the core signaling mechanisms which govern each state, are conserved among species. Jacob Hanna and colleagues continue this theme when they describe the establishment of a naïve human pluripotent state as an example of epigenetic reprogramming from primed pluripotency.

Post-implantation cellular reprogramming can be observed in a variety of contexts. To shed light on this, Magdalena Zernicka-Goetz and Chuen Yan Leung detail the genetic, morphological and physiological characteristics of the earliest stages of mouse embryogenesis, the knowledge of which is key to understanding how the process can be reversed or harnessed for direct conversion. Towards direct conversion, Sophia Péron and Benedikt Berninger present evidence that glia can be converted directly *in vivo* and *in vitro* into a neurogenic population by transcription factors, while Vania Broccoli and others review what is known about the unique set of histone modifications found in neural stem cells, and during direct conversation into neurons. Along the same lines, direct conversion with transcription factors is also being used to reprogram mesodermal lineages, where Jessica Vanslambrouck and Melissa Little detail the course required to create kidney nephron progenitor cells from adult kidney cells and Deepak Srivastava and Pengzhi Yu, describe the direct reprogramming of fibroblasts into induced cardiomyocyte-like cells.

Cellular programming and reprogramming are intricately linked to metabolic processes, and the transcriptional, epigenetic and metabolic state influence each other continuously. A particularly well-understood level of control is realized at the RNA level, with Ruth Lehmann and colleagues describing the functions of small RNA pathways in perhaps the best-studied system for RNA-mediated control, the Drosophila germ line. Similarly, Jason Doles and Bradley Olwin discuss how quiescent muscle stem cells use post-transcriptional regulatory networks to rapidly deploy the activation and proliferation program. At a more general level, Alessandro Brombin, Jean-Stéphane Joly and Françoise Jamen provide new insights into how ribosomes act as 'filters' to create translational specificity. Finally, we return to the more practical aspects of reprogramming and pluripotency, with Sean Palecek and colleagues reporting on how to utilize preprogrammed cells by giving an overview of microfluidics technology.

We trust these stimulating review articles will effect a little reprogramming of their own on perspectives in the field.